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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.                | CONFIRMATION NO.            |
| 10/574,034  | 05/02/2007  | Robert Bucki         | 46406-0109-01US<br>[222641]        | 9154                        |
| 23973 7590 04/07/2011<br>DRINKER BIDDLE & REATH<br>ATTN: INTELLECTUAL PROPERTY GROUP<br>ONE LOGAN SQUARE, SUITE 2000<br>PHILADELPHIA, PA 19103-6996 |             |                      | EXAMINER<br>DEVI, SARVAMANGALA J N |                             |
|   |             |                      | ART UNIT<br>1645                   | PAPER NUMBER                |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 10/574,034             | BUCKI ET AL.        |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | S. DEVI                | 1645                |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 January 2011.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 40-42 and 48-51 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 40-42 and 48-51 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)         | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

## **RESPONSE TO APPLICANTS' AMENDMENT**

### **Applicants' Amendment**

- 1) Acknowledgment is made of Applicants' amendment filed 01/24/11 in response to the non-final Office Action mailed 07/23/2010.

### **Status of Claims**

- 2) Claims 27-39 and 43-47 have been canceled via the amendment filed 01/24/11.

New claims 48-51 have been added via the amendment filed 01/24/11.

Claims 40-42 have been amended via the amendment filed 01/24/2011.

Claims 40-42 and 48-51 are pending and are under examination.

### **Prior Citation of Title 35 Sections**

- 3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

### **Prior Citation of References**

- 4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

### **Objection(s) Withdrawn**

- 5) The objection to the specification made in paragraph 7 of the Office Action mailed 07/23/10 is withdrawn in light of Applicants' amendment to the specification.
- 6) The objection to 40 made in paragraph 13 of the Office Action mailed 07/23/10 is withdrawn in light of Applicants' amendment to the claim.

### **Rejection(s) Withdrawn**

**7)** The rejection of claim 40 made in paragraphs 9(a), 9(b) and 9(e) of the Office Action mailed 07/23/10 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

**8)** The rejection of claim 42 made in paragraph 9(f) of the Office Action mailed 07/23/10 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

**9)** The rejection of claim 41 made in paragraph 9(g) of the Office Action mailed 07/23/10 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the base claim.

**10)** The rejection of claims 40-42 made in paragraph 12 of the Office Action mailed 07/23/10 under 35 U.S.C. § 102(b) as being anticipated by Rothenbach et al. (J. Appl. Physiol. 96: 25-31, January 2004, first published 02 May 2003. of record), is withdrawn in light of Applicants' amendment to the claims. A new rejection is set forth below to address the claims as amended and the newly added claims.

Applicants contend that claim 40 is directed to administering an amount effective for gelsolin to restore or maintain normal aggregation of platelets in the blood or extracellular fluid of the patient. Applicants state that Rothenbach et al. does not anticipate the claims as currently amended because Rothenbach et al. does not teach each and every limitation of the claimed invention and does not expressly teach a correlation between plasma gelsolin levels and platelet aggregation. Applicants submit that Rothenbach et al. investigated the role of plasma gelsolin in the pathophysiology of inflammation-induced lung injury (abstract); utilized a standardized rat burn model to induce a defined pulmonary injury and found that

plasma gelsolin depletion contributes to the pathophysiology of pulmonary vascular dysfunction. Applicants contend that even if the animals used in their study were subject to or susceptible to LPS-induced generalized coagulation dysfunction, there is no teaching in the Rothenbach et al. reference that administering exogenous plasma gelsolin restores blood platelet aggregation or a correlation between plasma gelsolin levels and restoration of platelet aggregation.

Applicants' arguments have been carefully considered, but are not persuasive.

Contrary to Applicants' assertion, Rothenbach et al. taught each and every structural element of the claims in complete detail, expressly and/or inherently, and therefore anticipate the claimed invention. See below under art rejections.

Applicants are referred to the same rebuttal on inherency as provided infra for the anticipatory rejection over Rosen et al.

### **Rejection(s) Maintained**

**11)** The rejection of claim 41 made in paragraph 9(c) of the Office Action mailed 07/23/10 under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein and herein below.

Although Applicants have provided sufficient antecedence to the identified limitations in lines 1 and 2 of the claim, the limitation 'extracellular fluid' in line 2 and the limitations 'gelsolin' in the last line continue to lack sufficient antecedence.

**12)** The rejection of claim 42 made in paragraph 9(d) of the Office Action mailed 07/23/10 under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for the reasons set forth therein and herein below.

Although Applicants have provided sufficient antecedence to the identified limitations in lines 1 and 2 of the claim, the limitation 'platelets' in line 2 continues to lack sufficient antecedence.

**13)** The rejection of claim 42 made in paragraph 9(g) of the Office Action mailed 07/23/10 under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for the reason set forth therein.

**14)** The rejection of claims 40-42 made in paragraph 11 of the Office Action mailed 07/23/10 under 35 U.S.C § 102(b) as being anticipated by Rosen et al. (WO 00/55350 A1, of record) as evidenced by Janmey et al. (J. Biol. Chem. 267: 11818-11823, 1992, of record) and Sheu et al. (Brit. J. Hematol. 103: 29-38, 1998, of record), is maintained for the reasons set forth therein and herein below.

New claim 51 is now added to this rejection.

Applicants submit the following arguments:

(a) To anticipate a claim, a reference must teach each and every element of the claim. (b) When a claim is directed to a combination of elements, it is not sufficient for the elements or limitations to merely be present somewhere within the prior art document, rather the combination itself must be specifically disclosed and not merely be part of a multitude of possibilities assembleable by piecing together elements mentioned in the disclosure of the prior art reference.

Richardson v. Suzuki Motor Company 868 F.2d 1226, 1236 (Fed.Cir. 1989) ("The identical invention must be shown in as complete detail as is contained in the patent claim."). (c) It is not sufficient for an anticipatory reference to merely recite individual elements of a claimed combination as part of long lists of possibilities without any suggestion or guidance leading one of ordinary skill in the art to make the specific combination claimed, as opposed to any other of a myriad

of possible combinations. *Minnesota Mining and Manufacturing Company v. Johnson & Johnson Orthopedics, Inc.* 976 F.2d 1559, 1572 (Fed.Cir. 1992). (d) Were the law otherwise, many novel and non-obvious inventions would be anticipated by many treatises, review articles, or even generalized references such as an encyclopedia, which may disclose the individual elements somewhere within the reference, but which do not teach with any specificity the particular inventive combination claimed. (e) The Court of Appeals for the Federal Circuit ('CAFC') has repeatedly held that for a reference to anticipate under 35 U.S.C. § 102, the reference must not only disclose all the elements of the claim within the four corners of the document, but must also disclose those elements "arranged as in the claim". A reference cannot be alleged to prove prior invention of a claimed subject matter and cannot anticipate under 35 U.S.C. § 102 unless the reference discloses within the four corners of the document not only all of the limitations of the claimed invention, but also all of the limitations arranged or combined in the same manner as recited in the claim, not merely in a particular order. *Net MoneyIn v. Verisign*, 545 F.3d 1359 (Fed. Cir. 2008). (f) *Rosen et al.* do not anticipate the claimed invention because they do not teach the specific claimed combination and do not show the instant invention in as complete detail as is contained in the claim. *Rosen et al.* disclose hundreds of cancer associated polypeptides and allege that the disclosed cancer associated polypeptides can be used to treat various diseases or conditions out of a long list of examples of diseases and conditions. Polypeptide of SEQ ID NO: 1065 is one of 842 human cancer associated polypeptides, and infectious diseases is one of the long list of medical conditions disclosed in *Rosen et al.* (g) Thus, the *Rosen* reference is not sufficient as an anticipatory reference because it merely recites individual elements as part of long lists of possibilities

without any suggestion or guidance leading one of ordinary skill in the art to make the specific combination claimed, as opposed to any other of a long list of alternative possibilities or myriad of possible combinations. Rosen et al. do not teach which polypeptides are effective for which diseases or conditions. Rosen et al. do not specifically teach using polypeptide of SEQ ID NO: 1065 to treat any particular condition, let alone LPS-induced generalized coagulation dysfunction. The reference must clearly and unequivocally disclose the claimed invention or direct a person of skill in the art to the invention without there being any need to pick, choose and combine various teachings of the cited reference. In re Arkley, 455 F.2d 586 (C.C.P.A. 1972).

Applicants' arguments have been carefully considered, but are not persuasive.

Contrary to Applicants' assertion, Rosen et al. taught each and every structural element of the claims in complete detail, expressly and/or inherently, and therefore anticipate the claimed invention. It is unclear what do Applicants mean by the statement that the claim is directed to a combination of elements, because instant claims are not directed to a combination of elements. It should be noted that the limitation 'to restore or maintain normal aggregation of platelets in the blood or extracellular fluid of the patient' in claim 40 represents the intended use of the claimed method. As set forth previously, Rosen et al. disclosed a method of treating medical conditions or infectious diseases, including Gram negative bacterial infections due to E. coli, such as sepsis or septic shock as well as septic shock comprising intravenous administration (i.e., administration into the blood) to a patient (i.e., a subject susceptible to LPS-induced generalized coagulation dysfunction) of a therapeutically effective amount of a polypeptide comprising

SEQ ID NO: 1065 (AAB43620), a fragment or an epitope thereof that has biological activity, i.e., functionally equivalent peptide fragment. See claim 17, section 'Infectious Disease' starting at page 403; pages 371, 372, 374, 375, 384 and 395; section 'Therapeutic/Prophylactic Administration and Composition' starting at page 336; pages 405 and 406; and pages 1051-1054. The prior art polypeptide is used to modulate blood coagulation disorders and blood platelet disorders such as thrombocytopenia and to decrease or dissolve clotting. See page 373. That thrombocytopenia is a hallmark of intravascular coagulation in a patient with Gram-negative bacterial sepsis and is due to LPS in patient's blood, which LPS enhances platelet aggregation, is inherent from the teachings of Rosen et al. in light of what is known in the art. For instance, Sheu et al. taught that thrombocytopenia is a hallmark of intravascular coagulation in a patient with Gram-negative bacterial sepsis and is due to LPS in patient's blood, which LPS enhances platelet aggregation. See right column on page 29. That the polypeptide, KHVVPNEVVVQRLFQVKGRR, representing amino acids 29-48 of the prior art SEQ ID NO: 1065 represents a biologically active gelsolin or a functionally equivalent peptide fragment of gelsolin and comprises Applicants' SEQ ID NO: 1 is inherent from the teachings of Rosen et al. in light of what is known in the art. For example, Janmey et al. taught the KHVVPNEVVVQRLFQVKGRR polypeptide sequence to correspond to amino acid residues 150-169 of gelsolin. See Table 1 of Janmey et al. Since all human or non-human patients with E. coli sepsis or septic shock are susceptible to LPS-induced generalized coagulation dysfunction, Rosen's patient is expected to be susceptible to LPS-induced generalized coagulation dysfunction. The Gram negative LPS-induced condition that is treated by Rosen's method, including infections due to E. coli (see for

example pages 404-406 of Rosen et al.) is the same condition that is recited as being used in the instant invention. See page 16 of Applicants' specification, for example. The QRLFQVKGRR peptide from within the above-identified gelsolin sequence, shows 100% literal identity to amino acids 160-169 of SEQ ID NO: 1 of the instant invention, and is therefore the same as Applicants' gelsolin sequence. Since the prior art gelsolin sequence is the same as the Applicants' gelsolin sequence, it necessarily possesses the same function as that of Applicants' gelsolin sequence, i.e., the capacity to maintain or restore normal aggregation of platelets. Applicants are reminded that '[p]roducts of identical chemical composition can not have mutually exclusive properties.' A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses in the specification and/or claims, i.e., the capacity to restore and maintain normal aggregation of platelets in blood or extracellular fluid of a patient, are necessarily present. The property of restoration or maintenance of normal aggregation of platelets in blood or extracellular fluid of a patient subject to or susceptible to LPS-induced generalized coagulation dysfunction is inseparable from the administered prior art gelsolin. Furthermore, the intravenous administration in the prior art method of the exogenous gelsolin sequence into the patient's blood in vivo necessarily increases the concentration of gelsolin therein compared to the level of gelsolin before administration. Thus, claims 40-42 are clearly anticipated by Rosen et al. The reference of Janmey et al. or Sheu et al. is not used as a secondary reference in combination with the reference of Rosen et al., but rather is used to show that every element of the claimed subject matter is disclosed by Rosen et al. with the unrecited limitation(s)

being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978).

With regard to Applicants' argument that Rosen et al. disclose hundreds of cancer associated polypeptides and that the disclosed cancer associated polypeptides can be used to treat various diseases or conditions out of a long list of examples of diseases and conditions, the following must be noted. A species which is specifically disclosed in a prior art reference is anticipatory even though it appears 'without special emphasis in a longer list'. *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1376 (Fed. Cir. 2005). As Rosen et al. taught that any polypeptide of their invention can be administered, it is anticipatory to the subject matter of instant claims, despite being a member of a list of other polypeptides. It must be noted that "[P]roof of efficacy is not required for a prior art reference to be enabling for purposes of anticipation." *Impax Laboratories Inc. v. Aventis Pharmaceuticals Inc.*, 468 F.3d 1366, 1382 (Fed. Cir. 2006). Thus, in this case, there is no legal requirement that Rosen et al. actually restore or maintain normal aggregation of platelets in blood; it is sufficient that Rosen et al. taught that it is used to modulate blood coagulation disorders and blood platelet disorders such as thrombocytopenia and to decrease or dissolve clotting. Applicants do not otherwise identify a defect in Rosen's disclosure that would prevent any polypeptide disclosed therein as being used in the manner described by Rosen et al.

With regard to Applicants' argument that the Rosen reference is not sufficient as an anticipatory reference because it merely recites individual elements as part of long lists of possibilities, the following must be noted. When the antibodies to the specific polypeptide species are taught, the claims are anticipated

no matter how many other antibody species are additionally named. Ex parte A, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990) (The claimed compound was named in a reference which also disclosed 45 other compounds. The Board held that the comprehensiveness of the listing did not negate the fact that the compound claimed was specifically taught. The Board compared the facts to the situation in which the compound was found in the Merck Index, saying that ‘the tenth edition of the Merck Index lists ten thousand compounds. In our view, each and every one of those compounds is described’ as that term is used in 35 U.S.C. § 102(a), in that publication.’). Id. at 1718. See also In re Sivaramakrishnan, 673 F.2d 1383, 213 USPQ 441 (CCPA 1982) (The claims were directed to polycarbonate containing cadmium laurate as an additive. The court upheld the Board’s finding that a reference specifically naming cadmium laurate as an additive amongst a list of many suitable salts in polycarbonate resin anticipated the claims. The applicant had argued that cadmium laurate was only disclosed as representative of the salts and was expected to have the same properties as the other salts listed while, as shown in the application, cadmium laurate had unexpected properties. The court held that it did not matter that the salt was not disclosed as being preferred, the reference still anticipated the claims and because the claim was anticipated, the unexpected properties were immaterial.).

With regard to Applicants’ statement on generalized references, which may disclose the individual elements somewhere within the references, the following must be noted. Extra references and extra evidence can be used to show that the primary reference contains an enabling disclosure and that a characteristic not disclosed in the reference is inherent. See MPEP 2131.01. ‘To serve as an anticipation when the reference is silent about the asserted inherent characteristic,

such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). Also note that the critical date of extrinsic evidence showing a universal fact need not antedate the filing date. See MPEP 2124. In the instant application, Applicants have failed to advance any arguments with regard to the extra evidence provided via the teachings of Janmey et al. or Sheu et al. Applicants have not identified any manipulative difference between Rosen's method and the claimed method. As discussed above, the claimed method is inherent and was in the public domain if it is the 'natural result flowing from' the explicit disclosure of the prior art" (*Perricone*, 432 F.3d at 1377), regardless of whether the inherent result is recognized. "It is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." In re *Woodruff*, 919 F.2d 1575, 1578 (Fed. Cir. 1990). When "a claimed new benefit or characteristic of an invention otherwise in the prior art" is an inherent property of the old invention, "the new realization alone does not render the old invention patentable." *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1377 (Fed. Cir. 2005). "[A] limitation or the entire invention is inherent and in the public domain if it is the 'natural result flowing from' the explicit disclosure of the prior art." *Id.*

(citations omitted). As summarized in *Perricone*, *id.* at 1375-76: A single prior art reference that discloses, either expressly or inherently, each limitation of a claim invalidates that claim by anticipation. *Minn. Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1565 (Fed. Cir. 1992). Thus, a prior art reference without express reference to a claim limitation may nonetheless anticipate by inherency. See *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349 (Fed. Cir. 2002). "Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claims limitations, it anticipates." *Id.* (quoting *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999)). Moreover, "[I]nherency is not necessarily coterminous with knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art." *Id.*; see also *Schering Corp. v. Geneva Pharms.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition in the prior art) (citing *In re Cruciferous Sprout Litig.*, 301 F.3d at 1351; *MEHL/Biophile*, 192 F.3d at 1366). "Thus, when considering a prior art method, the anticipation doctrine examines the natural and inherent results in that method without regard to the full recognition of those benefits or characteristics within the art field at the time of the prior art disclosure." *Id.* at 1378. See *Ex parte Satoshi Matsubara*, decided 02/10/2010, from Appeal 2009-006581.

Furthermore, it must be noted that it is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable. *In re Woodruff*, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent

properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs., 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP 2145. The rejection stands.

**Rejection(s) Necessitated by Applicants' Amendment**  
**Rejection(s) under 35 U.S.C § 112, Second Paragraph**

**15)** The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

**16)** Claims 40-42 and 48-51 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 40 is indefinite because the claim lacks sufficient antecedence in the limitation 'extracellular fluid'. See line 7. It is suggested that Applicants provide sufficient antecedent basis by replacing the limitation with --the extracellular fluid--.

(b) Claim 42 is indefinite because the claim lacks sufficient antecedence in the limitation 'platelets'. See line 2. Claim 42 depends indirectly from claim 40, which already includes this limitation. It is suggested that Applicants provide sufficient antecedent basis by replacing the limitation with --the platelets--.

(c) New claim 48 is indefinite and confusing in the limitation 'the gelsolin, or the functionally equivalent peptide fragment thereof, **comprises** plasma gelsolin', because it is unclear what are Applicants trying to convey [Emphasis added]. Does it mean that plasma gelsolin is 'comprised' within the

recited gelsolin or within the functionally equivalent peptide fragment thereof?

Clarification/correction is requested.

(d) Analogous rejection and criticism apply to claim 50 with regard to the limitation ‘the gelsolin, or the functionally equivalent peptide fragment thereof, **comprises** recombinantly produced or expressed gelsolin’ [Emphasis added].

(e) New claim 49 is indefinite and confusing in the limitation: the gelsolin, or the functionally equivalent peptide fragment thereof, comprises amino acid residues 160-169 of ‘gelsolin’. The recited amino acid residues 160-169 are from which gelsolin is unclear. Are these amino acid residues from a different gelsolin other than the earlier recited gelsolin, for example from a different animal species? If not, it is suggested that Applicants replace the limitation ‘gelsolin’ at the end of the claim with the limitation --the gelsolin--.

(f) Claims 41, 42 and 48-51, which depend directly or indirectly from claim 40, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim.

### **Rejection(s) under 35 U.S.C § 102**

**17)** The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**18)** Claims 40-42 and 48-51 are rejected under 35 U.S.C. § 102(b) as being anticipated by Rothenbach et al. (J. Appl. Physiol. 96: 25-31, January 2004, first published 02 May 2003, of record) as evidenced by Janmey et al. (J. Biol. Chem. 267: 11818-11823, 1992, of record).

Instant claims get the effective filing date of 11/12/2004 since the claimed invention is neither supported nor enabled in the provisional application filed 11/12/2003.

The preamble limitation ‘for restoring or maintaining normal aggregation of platelets in the blood ... in vivo’ represents the intended use of the claimed method. It is noted that the only required step of the claimed method is administering to the blood of a patient susceptible to or subject to LPS-induced generalized coagulation dysfunction a therapeutically effective amount of gelsolin or functionally equivalent peptide fragment thereof, to restore or maintain normal aggregation of platelets in the blood or extracellular fluid. It is further noted that microvascular dysfunction occurring during inflammation in trauma or burn patients is not excluded from the scope of ‘generalized coagulation dysfunction’ recited in claim 40. See for example, paragraph bridging pages 6 and 7 of Applicants’ specification.

Rothenbach et al. taught a method of intravenous infusion (i.e., in to the blood in vivo) of up to 7.8 mg (i.e., a therapeutically effective amount) of gelsolin to burn patients, i.e., rats (i.e., patients susceptible to LPS-generalized coagulation dysfunction), which resulted in attenuation of burn-induced pulmonary microvascular dysfunction in said patients. The burn-injured rat patients had decreased levels of plasma gelsolin before gelsolin infusion, and the intravenous infusion of exogenous gelsolin increased the plasma gelsolin level to normal plasma gelsolin levels. See title; abstract; ‘Methods’ on page 26; ‘Results’; Figure 1; page 28; and paragraph bridging pages 29 and 30. That the administered human plasma gelsolin of the prior art comprises therein a functionally equivalent peptide fragment of gelsolin and comprises Applicants’

SEQ ID NO: 1 is inherent from the teachings of Rothenbach et al. in light of what is known in the art. For example, Janmey et al. showed that the KHVVPNEVVVQRLFQVKGRR polypeptide sequence to correspond to amino acid residues 150-169 of gelsolin and thus comprises therein Applicants' SEQ ID NO: 1. See Table 1 of Janmey et al. Since the prior art product administered in to the blood of the patients susceptible to LPS-generalized coagulation dysfunction and the product administered in the instantly claimed method to a patient susceptible to LPS-generalized coagulation dysfunction is the same, i.e., gelsolin, both administered in a therapeutically effective amount, it necessarily possesses the same function as that of Applicants' gelsolin sequence, i.e., the capacity to maintain or restore normal aggregation of platelets. Note that '[p]roducts of identical chemical composition can not have mutually exclusive properties.' A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses in the specification and/or claims, i.e., the capacity to restore and maintain normal aggregation of platelets in blood or extracellular fluid of a patient, are necessarily present. Therefore, the prior art method that administers the same product necessarily results in the same effects as recited in the instant claims, i.e., restoration or maintenance of normal aggregation of platelets in the blood of the patients. Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

Claims 40-42 and 48-51 are anticipated by Rothenbach et al. The reference of Janmey et al. is **not** used as a secondary reference in combination with the reference of Rothenbach et al., but rather is used to show that every element of the claimed subject matter is disclosed by Rothenbach et al. with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978).

**19)** Claims 40-42 and 48-51 are rejected under 35 U.S.C. § 102(b) as being anticipated by Pepinsky et al. (WO 91/17170).

Pepinsky et al. taught a method for treating a patient having ARC, HIV infection, or AIDS (i.e., a subject susceptible to LPS-induced generalized coagulation dysfunction) comprising administering to the patient a therapeutically effective amount of a multimeric recombinant fusion composition comprising gelsolin moiety, having anti-coagulant or clot-dissolving catalytic activity, i.e., inhibition of platelet aggregation or maintenance of normal platelet aggregation. The gelsolin moiety used was human plasma gelsolin, or a biologically active fragment containing amino acids 160 to 169 of Applicants' SEQ ID NO: 1. See claim 51; first full paragraph on page 23; second full paragraph on page 6; the full paragraph on page 17; and the sequence alignment report below. The administration was via intravenous route. See paragraph bridging pages 32 and 33.

Has no US equivalents.

AAR15151

ID AAR15151 standard; protein; 23 AA.

AC AAR15151;

DT 25-MAR-2003 (revised)

DT 24-FEB-1992 (first entry)

DE GEL1 sequence.

KW Gelsolin; CD4; fusion protein; diagnosis; AIDS.

OS Synthetic.

FH Key Location/Qualifiers

FT Region 4. .23

FT /label= PIP2-binding\_sequence

FT /note= "amino acids 150-169"

PN WO9117170-A.  
PD 14-NOV-1991.  
PF 04-MAY-1990; 90US-00520368.  
PR 04-MAY-1990; 90US-00520368.  
PA (BIOJ ) BIOGEN INC.  
PI Pepinsky RB, Rosa MD, Stossel TP;  
DR WPI; 1991-353711/48.  
PT New multi-meric and hetero-multi-meric gelsolin fusion constructs - used  
PT to treat and diagnose AIDS, ARC and HIV infection.  
PS Example 2; Page 37; 131pp; English.  
CC Oxidized CD4(375) was reacted with the gelsolin moiety, GEL1. To verify  
CC that GEL1 had been crosslinked to CD4(375), selected fractions were  
CC analysed by Western blotting using antibodies against GEL1. A prominent  
CC immunoreactive band was observed in the sample after crosslinking. This  
CC band is absent from the Western blot of an untreated CD4 sample. See also  
CC AAQ14931-35 and AAR15151. (Updated on 25-MAR-2003 to correct PA field.)  
SQ Sequence 23 AA;

Query Match 100.0%; Score 50; DB 1; Length 23; Best Local Similarity 100.0%;  
Matches 10; Conservative 0; Mismatches 0; Indels 0; Gaps 0.

Qy 1 QRLFQVKGRR 10  
| | | | | | | |  
Db 14 QRLFQVKGRR 23

Claims 40-42 and 48-51 are anticipated by Pepinsky et al.

## Remarks

**22)** Claims 40-42 and 48-51 stand rejected.

In line 4 of claim 40, it is suggested that Applicants provide sufficient antecedent basis to the limitation 'extracellular fluid' by inserting the limitation -- the-- before the above-identified limitation.

**23)** Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the

advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

**24)** Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

**25)** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

**26)** Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

/S. Devi/  
Primary Examiner  
AU 1645

April, 2011